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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,073	07/17/2007	Yves Claude Nicolau	ACI-0403US	4203

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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/590,073	**Applicant(s)** NICOLAU ET AL.
	Examiner YUNSOO KIM	**Art Unit** 1644

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 06 March 2012 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

NO NOTICE OF APPEAL FILED

1. ☒ The reply was filed after a final rejection. No Notice of Appeal has been filed. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance;

(2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114 if this is a utility or plant application. Note that RCEs are not permitted in design applications. The reply must be filed within one of the following time periods:

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action; or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

c) ☐ A prior Advisory Action was mailed more than 3 months after the mailing date of the final rejection in response to a first after-final reply filed within 2 months of the mailing date of the final rejection. The current period for reply expires months from the mailing date of *the prior Advisory Action* or SIX MONTHS from the mailing date of the final rejection, whichever is earlier.

Examiner Note: If box 1 is checked, check either box (a), (b) or (c). ONLY CHECK BOX (b) WHEN THIS ADVISORY ACTION IS THE FIRST RESPONSE TO APPLICANT'S FIRST AFTER-FINAL REPLY WHICH WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. ONLY CHECK BOX (c) IN THE LIMITED SITUATION SET FORTH UNDER BOX (c). See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) or (c) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendments filed after a final rejection, but prior to the date of filing a brief, will not be entered because

a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);

b) ☐ They raise the issue of new matter (see NOTE below);

c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☒ Applicant's reply has overcome the following rejection(s): new matter rejection see office action mailed 1/6/12 sections 10-12.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): (a) ☐ will not be entered, or (b) ☒ will be entered, and an explanation of how the new or amended claims would be rejected is provided below or appended.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing the Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

12. ☒ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). 3/6/12

13. ☐ Other: _____.

STATUS OF CLAIMS

14. The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: .

Claim(s) objected to: .

Claim(s) rejected: 19,20,23,25,26,29-32.

Claim(s) withdrawn from consideration: .

/Yunsoo Kim/
Primary Examiner, Art Unit 1644

Continuation of 11. does NOT place the application in condition for allowance because:

1. Claims 19, 20, 23, 25, 26 and 28-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of restoring memory and curiosity awakening by administering supramolecular antigenic construct comprising an antigenic peptide set forth in SEQ ID NO:1-6 with palmitoylation and pegylation, does not reasonably provide enablement for methods to restoring memory and curiosity awakening by administering any supramolecular antigenic constructs comprising any active fragments of amyloid or any peptides of GXXXGXXXGG or GXXXG motifs.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed.Cir.1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of the skilled in the art to practice the claimed invention.

The claimed is drawn to the method of improving pathological conditions (e.g. memory restoration and curiosity awakening) of Alzheimer's disease comprising administering a supramolecular constructs of any GXXXGXXXGG or GXXXG peptide motifs and the construct may be used in treating disorders comprising Alzheimer's disease. Wolf-Klein et al teaches that there is no medical treatment currently available to cure of stop the progression of Alzheimer's disease (Wolf-Klein et al., Am Journal of Hosp Palliat Care, 2007, 24(1):77-82, abstract, in particular, of record) despite of current pharmaceutical advances in delaying disease progression. Even though there are five FDA approved Alzheimer's drugs, they temporarily relieve some symptoms of the diseases. Further, Wolf-Klein et al. discloses that the length of survival has not changed despite new technology and therapeutic approaches and the tolls of this incurable disease continue to increase (abstract, p. 77, 2nd col.)

In addition, Applicants have not provided any in vivo working examples that the supramolecular constructs with fragments Aβ peptides and peptides of GXXXGXXXGG or GXXXG motifs can be used in methods of restoring memory and curiosity awakening.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed supramolecular constructs in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. In re Fisher, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Applicant's response and amendments to the claims filed on 3/6/12 have been fully considered but they were not persuasive.

Applicant has asserted that the restoring of memory by administration of supramolecular constructs of amyloid peptides are known in the art and Applicant has referenced Muhs et al. (PNAS, 2007, vol. 104, p. 9810-9815).

As Applicant has acknowledged, Muhs et al. discloses efficacy of liposomal based vaccine comprising the amyloid peptide 1-15 (Aβ1-15). The prior art peptide is relevant to support the claimed SEQ ID NO:1-6 but does not support any active fragments of Aβ peptides or peptides having GXXXGXXXGG or GXXXG motifs.

Contrary to Applicant's assertion, the claimed invention is not limited to restore memory and curiosity awakening by administration of supramolecular construct having the SEQ ID NO:1-6 rather the claimed method encompasses other unspecified fragments of Aβ peptides and GXXXGXXXGG or GXXXG peptide motifs. As discussed above, Wolf-Klein et al teaches that there is no medical treatment currently available to cure or stop the progression of Alzheimer's disease (Wolf-Klein et al., Am Journal of Hosp Palliat Care, 2007, 24(1):77-82, abstract, in particular, of record) despite of current pharmaceutical advances in delaying disease progression. Even though there are five FDA approved Alzheimer's drugs, they temporarily relieve some symptoms of the diseases. Further, Wolf-Klein et al. discloses that the length of survival has not changed despite new technology and therapeutic approaches and the tolls of this incurable disease continue to increase (abstract, p. 77, 2nd col.). Moreover, the specification of the instant application in p. 3 acknowledges that the delaying and reversing the progression is largely unsuccessful. The specification of the instant application states:
The management of AD consists of medication-based and non-medication based treatments. Treatments aimed at changing the underlying course of the diseases (delaying or reversing the progression) have so far been largely unsuccessful.

For the reasons addressed previously, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed supramolecular constructs in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. In re Fisher, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

2. Claims 19, 20, 23, 25, 26 and 28-32 are rejected under 35. U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of supramolecular antigenic constructs wherein the antigenic construct is a SEQ ID NOs:1-6 with a modification such as palmitoylation; however, Applicant is not in possession of any supramolecular antigenic constructs comprising any unspecified amyloid peptide motifs including GXXXG and GXXXGXXXGG or any fragments thereof.

The claims broadly encompass any peptides from any amyloid proteins in any lengths. The specification does not provide written description for such broad genus peptide encompassed by the claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The guidelines of the Examination of Patent Applications Under the 35 U.S.C. 112 § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e.., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Fri. January 5, 2001, see especially page 1106, column 3).

The antigenic peptide of the instant claims is drawn to any peptide that is obtained from any amyloid protein and some may have GXXXG and GXXXGXXXGG motifs. The specification of the instant application discloses some peptides (as in claim 25) that are derived from Aβ amyloid. However, the claimed peptide is not limited to Aβ amyloid but encompasses any amyloid proteins and the fragments thereof. It is noted that amyloid is defined as any complex protein that is deposited in tissues and shares selected laboratory features such as a change in the fluorescence intensity of certain aromatic dyes (Medicine Net definition, 8/8/04, of record) and there are number of other amyloids does not have any structural relationship with Aβ amyloid (wikipedia, 2009, p. 1-6, of record). Given that the broad range of peptides is claimed, it is apparent that the instant specification fails to disclose any species of peptides that are non Aβ amyloid. Thus, the failure of disclosure is not sufficiently representative of the broad genus of structurally different antigenic peptides other than Aβ amyloid sequences of claim 25.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant's arguments filed on 3/6/12 have been fully considered but they were not persuasive.

Applicant has asserted that the current claim amendment obviates the rejection as the antigenic fragments are SEQ ID NOs:1-5 and this satisfies the representative number of species..

Contrary to Applicant's assertion, the claimed peptide is not limited to β amyloid or fragments set forth in the SEQ ID NOs:1-6 but includes any antigenic polypeptide that encompassed by any fragments of β amyloid and other unspecified amino acid sequences in addition to the β amyloid sequence and the sequences encompassed by the GXXXG and GXXXGXXXGG motifs. Given that the broad range of peptides is claimed, it is apparent that the instant specification fails to disclose any species of antigenic peptides that comprise any fragments of β amyloid and unspecified amino acids or structural motifs set by GXXXG and GXXXGXXXGG other than SEQ ID NO:1-6. Thus, the failure of disclosure is not sufficiently representative of the broad genus of structurally different antigenic peptides other than β amyloid sequences of claim 25.

3. Claims 19, 20, 23, 25, 26 and 28-32 stand rejected under 35 U.S.C. 102(b) as being anticipated by Nicolau et al. (PNAS, 2002 vol. 99, no. 4, p. 2332-2337, IDS reference, of record) for the reasons set forth in the office action mailed on 7/6/11.

Nicolau et al. teach administration of antigenic composition comprising a peptide comprising the claimed SEQ ID NO:1 in a reconstituted liposome comprising phospholipids and cholesterol (Fig.1, p. 2333) in PBS (e.g. pharmaceutical carrier). Further, Nicolau et al. teach that a hydrophobic (e.g. palmitoylic acid) tail is attached to a lysine residue of the peptide (Introduction, p. 2332) and the peptide is derived from Aβ amyloid sequence.

Claims 28-30 are included in this rejection because the SEQ ID NO:1 has GXXXG and GXXXGXXXGG motifs as is evidenced by the specification of the instant application in p. 25-26.

Given that the identical antigenic composition is administered to a group of subject having Aβ plaques (p. 2333, col. 2), the referenced composition inherently enhances the antigenicity in a patient of Alzheimer's disease.

Even if the claimed method does not recite a particular patient population, the patient population having Aβ plaques cannot be excluded from the study because having Aβ plaques is considered as indication of Alzheimer's disease (p. 2332). Thus, prior art population and the potential population of the claimed method are considered identical. Therefore, the reference teachings anticipate the claimed invention.

Applicant's arguments filed on 3/6/12 have been fully considered but they were not persuasive.

Applicant has asserted that the Nicolau et al. is not a proper anticipatory reference as the reference fails to teach memory restoration and curiosity awakening and this is not enabling by the Nicolau reference (p. 11 of the response filed on 11/7/11 based on p.2337 of Nicolau). The current claim set recites the method for "restoring memory and curiosity awakening" and Applicant has addressed that this is an important therapeutic effect on the brain during the telephonic interview held on 10/27/11.

Applicant has further asserted that the Nicolau et al. express serious doubt to the NOBRA mouse model in the treatment of Alzheimer's diseases because the NOBRA model does not provide a blood-brain barrier to cross for the antibodies to reach the pancreatic plaques. Applicant has traversed that the Nicolau et al. do not provide any evidence that the antigenic structures for clearing plaques from the brain based in vitro data of Fig 4.

Contrary to Applicant's assertion, the currently claimed construct used in the claimed method and the prior art construct are identical. Given that the identical composition to the claimed invention is being administered to the same patient population, the administration of the composition will inherently achieve the intended purpose of the claimed invention - restore memory restoration and curiosity awakening. However, it is noted that the structure of the claimed invention can be differentiated from the prior art structure. As disclosed in specification in p. 22 of the instant application, the claimed invention may be further described to add peg moieties in addition to the palmitoylation of in the lysine residue of the structure of the Nicolau reference. This distinction may be critical to support the currently amended intended use of the supramolecular construct in restoring memory and curiosity awakening by crossing the blood-brain barrier while the construct lacking the pegylation may not able to achieve such functions.

As the currently amended claims do not specify the structural differences between the claimed supramolecular construct and the prior art construct (both recite antigenic peptide and hydrophobic moieties), the claimed supramolecular construct would inherently achieve the intended use of the claimed method. Therefore, the reference teachings anticipate the claimed invention and the rejection is maintained.